IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

#11
Plunkett
11/2/00

Application of: Johnson

Serial No.: 09/158,120

Filed: September 21, 1998

For: Human-Murine Chimeric Antibodies Against Respiratory Syncytial Virus

Group: 1644

Examiner: Ewoldt

Assistant Commissioner of Patents
Washington, D.C. 20231

Sir:

In response to the Office Action dated April 26, 2000, reconsideration of the above-identified application is hereby respectfully requested.

Claims 1-4 and 21 stand rejected under 35 U.S.C. 102(a) as being anticipated by Tempest, et al.

Claims 1-4, 6, 7, and 21 stand rejected under 35 U.S.C. 103 as being unpatentable over Tempest, et al. in view of Beeler, et al.

Claims 1-4, 6, 7, and 21 stand rejected under 35 U.S.C. 103 as being unpatentable over Jones, et al. in view of Beeler, et al.

These rejections are respectfully traversed.

The present invention is one aspect, as defined in Claim 1, is directed to a human-murine antibody against respiratory syncytial virus. The antibody comprises a human antibody containing at least one CDR from each of the variable heavy and variable light chains of a murine monoclonal antibody against respiratory syncytial virus.

In another aspect, as defined in Claim 21, there is provided an antibody against respiratory syncytial virus which comprises a human constant region, a heavy chain and light chain variable region, each of which comprises a framework region, at least a portion of which is human, and three complementary determining regions. Each complementary determining region is derived from a murine monoclonal antibody.

With respect to the Tempest reference, Applicant, in parent Application Serial No. 08/290,592, now U.S. Patent No. 5,824,307, submitted a Declaration Under 37 CFRI.131 of Leslie S. Johnson. In such Declaration, Applicant stated that Applicant conceived the present invention prior to March 1991, the effective date of the Tempest reference, and from such conception, diligently worked to reduce the invention to practice. Therefore, Tempest no longer is an effective reference against the above-identified application under 35 U.S.C. 102(a) or 35 U.S.C. 103.

Beeler discloses only murine monoclonal antibodies. It does not disclose or even remotely suggest to one of ordinary skill in the art human-murine antibodies. Furthermore, Beeler does not disclose or even remotely suggest to one of ordinary skill in the art humanized antibodies of any sort. Especially, Beeler does not disclose or suggest to one of ordinary skill in the art which, if any murine monoclonal anti-RSV antibodies could be humanized and retain vital neutralization properties at therapeutically effective levels.

In view of the above, the human-murine antibodies of the invention are patentable over Beeler.

Regarding the Jones reference, Jones does not disclose or even remotely suggest to one of ordinary skill in the art the use of CDRs with specificity to any RSV antigen. Jones did not use the CDRs from both the variable heavy and variable light chains. In Jones, only a mouse V_h CDR was grafted into a human heavy chain framework region. Furthermore, Jones only

examined antigen binding, comparing the binding of the mouse monoclonal and polyclonal MVnp anti-idiotypic antibodies. The difference in affinity to the anti-idiotypic antibody only shows that the CDR has lost certain determinants in the humanized antibody. Also, Jones provides no suggestion that the antibodies of Jones are useful for use in human therapy. Jones, therefore, does not render Applicant's claimed antibodies obvious to one of ordinary skill in the art.

Jones and Beeler, therefore, alone or in combination, do not disclose or even remotely suggest Applicant's claimed human-murine antibodies to one of ordinary skill in the art, and thus do not render Applicant's claimed human-murine antibodies obvious to one of ordinary skill in the art. It is therefore respectfully requested that the rejections under 35 U.S.C. 103 be reconsidered and withdrawn.

Claim 6 stands rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to convey reasonably to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. This rejection is respectfully traversed.

The Examiner has taken the position that the specification only provides a written description of antibodies which are specific for site C of RSV protein F, and that there is insufficient written description of an antibody specific for antigenic site A of RSV protein F.

Applicant respectfully disagrees. The specification, at Page 5, lines 1-5, states that the murine antibodies against RSV F antigen, which are used in making the human murine antibodies of the present invention, have been mapped to the A, B, and C antigenic sites of the RSV F antigen. The epitopes in Sites A and C have shown the least variability in natural isolates.

The specification does show, through working examples, that one can construct a human-murine antibody in accordance with the invention which is specific for antigenic site C of RSV F antigen. Because Applicant has shown that one can construct a human-murine antibody specific for antigenic site C of the RSV F antigen, one skilled in the art also would expect reasonably that one could construct a human-murine antibody in accordance with the invention that is specific for antigenic site A of the RSV F antigen. Applicant has proven the principle that one can construct a human-murine antibody in accordance with the present invention. The Examiner has provided no evidence other than sheer speculation that would indicate to one skilled in the art that antibodies other than those disclosed specifically could not be constructed. Because the Examiner has provided no evidence that a human-murine antibody, which is specific for antigenic site A of the RSV F antigen as defined in Claim 6, cannot be constructed, the Examiner has not demonstrated that Claim 6 is not enabled. It is therefore respectfully requested that the rejection under 35 U.S.C. 112, first paragraph, be reconsidered and withdrawn.

Claims 2 and 4 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to point out particularly and claim distinctly the subject matter which Applicant regards as the invention. This rejection is respectfully traversed.

The Examiner states that Claims 2 and 4 are indefinite in the recitation of "neutralizing antibody." In response, Applicant asserts that the term "neutralizing antibody" is understandable readily by those skilled in the art. Because the term "neutralizing antibody" is understood readily by those skilled in the art, Claims 2 and 4 clearly define the metes and bounds of the invention defined therein.

Therefore, Claims 2 and 4 point out particularly and claim distinctly by the subject matter Applicant regards as the invention, and it is therefore respectfully requested that the rejection under 35 U.S.C. 112, second paragraph, be reconsidered and withdrawn.

With respect to the obviousness-type double patenting rejection over the '307 patent, Applicant submits a terminal disclaimer with this response.

For the above reasons and others, this application is in condition for allowance, and it is therefore respectfully requested that the rejections be reconsidered and withdrawn and a favorable action is hereby solicited.

Respectfully submitted

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